Proangiogenic Collagen-Binding Glycan Therapeutic Promotes Endothelial Cell Angiogenesis.

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Public Summary:

Scientific Abstract:
Stimulating angiogenesis during wound healing continues to present a significant clinical challenge, given the limitations of current strategies to maintain therapeutic doses of growth factors and endothelial cell efficacy. Incorporating a balance of specific cues to encourage endothelial cell engraftment and cytokines to facilitate angiogenesis is necessary for blood vessel growth in the proinflammatory wound environment. Here, we incorporate a previously designed peptide (LXW7) capable of binding to the alphavbeta3 integrin of endothelial cells with a dermatan sulfate glycosaminoglycan backbone grafted with collagen-binding peptides (SILY). By exploiting alphavbeta3 integrin-mediated VEGF signaling, we propose an alternative strategy to overcome shortcomings of traditional growth factor therapy while homing the peptide to the wound bed. In this study, we describe the synthesis and optimization of LXW7-DS-SILY (LDS) variants and evaluate their angiogenic potential in vitro and in vivo. LDS displayed binding to collagen and endothelial cells. In vitro, the LDS variant with six LXW7 peptides increased endothelial cell proliferation, migration, and tubule formation through increased VEGFR2 phosphorylation compared to nontreated controls. In an in vivo chick chorioallantoic membrane assay, LDS laden collagen hydrogels increased blood vessel formation by 43% in comparison to the organism matched blank hydrogels. Overall, these findings demonstrate the potential of a robust targeted glycan therapeutic for promoting angiogenesis during wound healing.